

**REMARKS**

Claims 1, 3, 6, 7 and 12-16 are pending. Claim 1 is amended. The support for claim 1 amendments may be found throughout the specification as filed and specifically at page 5, lines 9-10 and Figure 7. Also, as requested by the Examiner, a period after ‘lipase’ is removed in overcome Examiner’s claim objections. Thus, no new matter has been added.

**35 U.S.C. § 112, second paragraph.**

Claims 1, 3, 6, 7, 12, 13 and 16 were rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter. In view of amendments to claim1, Applicants request reconsideration and withdrawal of the rejection.

**35 U.S.C. § 102(b)**

Claims 1, 3, 6, 12, 13 and 16 are rejected as being allegedly anticipated by Kabalka et al., (Mag. Res. in Medicine, 1991), “Kabalka”. In order to anticipate a claim, a single prior art reference must disclose each and every limitation of the claim. MPEP 2131. In view of amendments to claim 1 and remarks presented below, Applicants respectfully request reconsideration and withdrawal of the rejection.

The instant methods comprises *inter alia* using insoluble particles that are per se “relaxometrically silent”, i.e. unable to create contrast, when used in T1-weightend sequences. In fact, only after being exposed to cells, internalized inside them and then locally degraded by specific enzymes, the said particles release the relaxometrically active species, namely single units of paramagnetic chelate, creating the contrast in the resulting images.

Kabalka relates to gadolinium-labeled liposomes containing paramagnetic contrast agents which are specifically targeted for liver. Examiner contends at page 4 of the Office Action, that Kabalka liposomes “containing paramagnetic amphiphilic agents significantly enhance the signal intensity in T1-weighted MRI”. Thus, contrary to the instant insoluble particles, the liposomes used in Kabalka are *per se* relaxometrically active and do not require any enzymatic activation to provide the enhanced signal.

Applicants urge that Kabalka does not teach or suggest an instant method comprising the use of relaxometrically silent insoluble particle. In view of remarks provided above, Applicants request reconsideration and withdrawal of the § 102(b) rejection.

### **35 U.S.C. § 103**

Claims 1, 3, 6, 7, 12 and 13 were rejected as obvious over the combination Kabalka et al. (Mag. Res. in Medicine, 1988, 8, 53, page 89-95, “Kabalka”) in view of Ranney (U.S.5,155,215, “Ranney”). In view of the amendments to claim 1 and remarks presented below, Applicants request reconsideration and withdrawal of the rejection.

In order to establish obviousness, it is necessary, *inter alia*, to (i) determine the scope of the prior art and (ii) the differences between the claimed subject matter and that of the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Furthermore, a *prima facie* finding of obviousness cannot be established when the “improvement is more than the predictable use of prior art elements according to their established functions.” *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct 1727, 1739 (2007). A reasonable expectation of success is required. MPEP 2143.02. Unexpected, *i.e.* surprising, results rebut a *prima facie* case of obviousness. MPEP 2144.09.

Applicants respectfully traverse the § 103(a) rejection because, for the reasons discussed below, the cited combination fails to teach or suggest all of the claim limitations.

*The Cited Combination Fails to Teach or Suggest All of the Claim Limitations*

Kabalka relates to gadolinium-labeled liposomes containing paramagnetic contrast agents which are specifically targeted for liver. As described above, in view of amendments to claim 1 and remarks presented herein, Kabalka does not teach or suggest instant method comprising the use of relaxometrically silent insoluble particles.

Ranney does not remedy the deficiency of Kabalka. Ranney relates to image-enhancing agents, contrast agents or spectral shift agents to enhance tissue or organ images or nuclear spectra obtained with radioisotope scanning or NMR imaging or spectroscopy. Ranney does not teach or suggest an instant method comprising the use of relaxometrically silent insoluble particles.

Therefore, for the above reasons, Applicants respectfully request withdrawal of the obviousness rejection over Kabalka in view of Ranney.

**Conclusion**

Therefore, for the above reasons, applicants submit that the presently pending claims are in condition for allowance and request the speedy issuance of a notice of allowability.

No fee, except a fee accompanied an RCE, is believed to be due for the filing of this Amendment and Response to Final Office Action. However, the Director is hereby authorized to charge any required fees and credit any overpayments to Deposit Account No. 50-0540.

Respectfully submitted,

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